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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,293	04/15/2005	David Dunger	102657-102	6369

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WIGGIN AND DANA LLP
ATTENTION: PATENT DOCKETING
ONE CENTURY TOWER, P.O. BOX 1832
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EXAMINER	
SAOUD, CHRISTINE J	
ART UNIT	**PAPER NUMBER**
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/507,293	DUNGER ET AL.	
	Examiner	Art Unit	
	Christine J. Saoud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2004 (preliminary amendment*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-8,10,11 and 13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-8, 10, 11 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/9/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's preliminary amendment, filed 09 September 2004, has been received and entered. Claims 1-5, 9, and 12 have been canceled. Claims 6-7, 10-11, and 13 have been amended. Claims 6-8, 10-11 and 13 are currently pending and under examination.

Priority

If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. 120, a specific reference to the prior-filed application in compliance with 37 CFR 1.78(a) must be included in the first sentence(s) of the specification following the title or in an application data sheet. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications.

If the instant application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. **If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen**

months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37

CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 recites the limitation "to a patient suffering therefrom during the evening". This language seems to imply that the patient is suffering from diabetes only during the evening. The "during the evening" limitation should most likely be referring back to the administration of the insulin and pegvisomant. This could be accomplished by reciting

"to said patient wherein said administering is performed during the evening" or something similar.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. .

Claim 7 recites "administering to the patient a daily dose of the GH antagonist pegvisomant and less frequent overnight infusions of insulin together with a hyperinsulinaemic euglycaemic clamp". However, the "hyperinsulinaemic euglycemic clamp" is a test for investigating and quantifying insulin resistance. It measures the amount of glucose necessary to compensate for an increased insulin level without causing hypoglycemia. The test is rarely performed in clinical care, but is used in medical research. Therefore, it is not an accepted method of treating diabetes and would not be considered a method of treating diabetes because it is a tool for testing insulin resistance. Therefore, the claims are not enabled for a method of reducing the overnight insulin requirement of a patient with diabetes with a hyperinsulinaemic euglycaemic clamp.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6, 10-11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Atiea et al. (J. Clin. Endocrinol. Metab. 69(2): 390-395, 1989) in view of Goffin et al. (Pharmapress. 3(5): 752-757, 2002).

Atiea et al. teach that patients suffering from insulin-dependent diabetes mellitus (IDDM) experience an early morning rise in plasma glucose. This phenomenon referred to as dawn phenomenon. Dawn phenomenon results in early morning hyperglycemia and in increases in the insulin requirement. Atiea et al. also teach that growth hormone (GH) is a major factor in the pathogenesis of the dawn phenomenon since suppression of GH by native somatostatin leads to a significant reduction in early morning plasma glucose concentrations (see page 390, column 1, paragraph 1). Atiea et al. teach that

GH is causally related to the dawn phenomenon and that its suppression may reduce early morning hyperglycemia (see page 394, column 1, final paragraph). Atiea et al. do not teach a method of reducing overnight insulin requirement of an IDDM patient comprising administering insulin and the growth hormone antagonist pegvisomant.

Goffin et al. teach that pegvisomant is a polyethylene glycol derivative of human growth hormone that acts as a highly selective GH receptor antagonist. Pegvisomant binds the hGH receptor but acts as an inactive competitor with endogenous hGH and blocks hGH receptor-mediated actions. Goffin et al. also teach a dosing range of 1 to 10 mg/kg/day reduced circulating IGF-1 levels, with maximal effect up to 70% of control values, which is a measure of a physiological dose (see page 753, column 1, final paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to treat patients with IDDM at night with insulin and pegvisomant in order to reduce the overnight requirements for insulin and reduce dawn phenomenon because Atiea et al. teach that patients with IDDM suffer from an early morning rise in plasma glucose, which requires insulin and that this phenomenon is caused by increased GH secretion at night and that this phenomenon can be suppressed by decreasing GH secretion. Goffin et al. teach an agent which blocks the activity of GH, pegvisomant, by binding the GH receptor and preventing the activation of the receptor by exogenous GH. One of ordinary skill in the art would be motivated to administer the GH antagonist, pegvisomant, of Goffin et al. in order to block/suppress the actions of endogenous GH which are known to cause dawn phenomenon as taught by Atiea. One

has a reasonable expectation of success in reducing the overnight insulin requirement in IDDM patients by this method because the insulin requirement is increased overnight by the dawn phenomenon, which would be reduced by the blocking of GH action. Addtionally, Goffin et al. teach a dosage range that would be expected to have a physiological effect on growth hormone levels which meets the limitations of the dosages in the claims. Therefore, the invention as instantly claimed would have been prima facie obvious to one of ordinary skill in the art to which it pertains, absent evidence to the contrary.

Claims 7-8 are not included in this ground of rejection because use of a hyperinsulinaemic euglycaemic clamp is not considered a treatment method for IDDM patients for the reasons stated in the rejection under 112/1st paragraph.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud whose telephone number is 571-272-0891. The examiner can normally be reached on Monday-Friday, 6AM-2PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CHRISTINE J. SAOUD
PRIMARY EXAMINER
Christine J. Saoud